

particular, the pressure may range from 0.3 to 1 atm and even exceed 1 atm. Even  $P=0.3$  atm allows ESI (in the form of SPIN sources) and IMS/MS to perform virtually as well as at ambient pressure.

As detailed herein, extensive characterization of  $2^{nd}$ -generation ion funnels has proven the theory that the maximum operating pressure scales with  $w$  and  $A$ . The underlying physics has no pressure limit and must equally apply up to  $P=1$  atm and beyond. Then effective ion focusing at  $P=1$  atm (or  $\sim 25$  times the present value of  $P=30$  Torr) would require  $w \sim 50$  MHz and, in the current funnel geometry,  $U=5$  kV or  $A=100$  kV/cm. Reaching those values would necessitate augmenting the electrical power output by  $25^4=390,625$  times, an impossible proposition from either the power consumption or heat release viewpoints. Also, the breakdown voltage for a 0.5-mm gap at  $P=1$  atm is  $\sim 2$  kV in  $N_2$  or air and much lower in He gas and He/ $N_2$  mixtures with 50-75% He that are critical to high-resolution FAIMS and many IMS applications in structural biology and other areas. Hence a hypothetical funnel with  $g=0.5$  mm and  $U=5$  kV would instantly break down even in  $N_2$  or air, let alone He-containing gases.

In terms of field intensity, the breakdown threshold for any gas increases in narrower gaps. In particular, by the Paschen law, gaps of  $g=35$   $\mu$ m can sustain  $A$  up to  $\sim 170$  kV/cm, or  $\sim 170\%$  of the value theoretically necessary for focusing at  $P=1$  atm. Operation at  $\sim 80\%$  of the breakdown voltage tends to be very stable, thus the factor of 1.7 provides headroom to increase  $A$  above the projected 100 kV/cm (if necessary) while ensuring system stability. Experimentally, electrode stacks with gaps of  $g=35$   $\mu$ m at ambient pressure easily support RF electric fields with  $w \sim 30$  MHz and  $A$  of at least 60 kV/cm, or  $>50\%$  above the maximum  $A$  for  $g=0.5$  mm. Experiments detailed herein demonstrate that the above remains true in He;  $N_2$  mixtures and He gas. For example, FIG. 3a and FIG. 3b shows the total FAIMS and MS spectra (respectively) obtained for the tryptic digest of bovine serum albumin in He using a microchip with  $g=35$   $\mu$ m,  $A \sim 60$  kV/cm, and  $w=28.5$  MHz. These data indicate that  $A \sim 100$  kV/cm can be established in He/ $N_2$  with high He content, if not pure He. Experimentally, the electrode stacks of the FANS microchip allow harmonics with  $w$  of at least 57 MHz, which exceeds what we estimate here as needed for focusing at  $P=1$  atm. Thus, RF fields of a frequency and amplitude needed to operate the present invention can be maintained even in the He gas.

Chip-based devices in accordance with the invention, with microscopic gaps between electrodes, focus ions using the Dehmelt potential of a symmetric RF field. With  $g < 100$   $\mu$ m and particularly  $\sim 75$   $\mu$ m, such devices can deliver RF fields of unprecedentedly high frequency and intensity that theoretically suffice for ion focusing at ambient pressure or near-ambient pressure, within the capability envelope of RF power supplies known in the art and without electrical breakdown in the gas. Formulation of this previously unrealized feasibility is central to the Invention.

The above linear scaling of  $P$  with  $w$  and  $A$  applies to still gas, when the flow drag on ions does not materially affect their dynamics in RF fields. That is the case with current funnel implementations inside and at the terminus of IMS drift tubes where the gas flow if any is uniform and slow, but not at API/MS interfaces where ions in a supersonic jet expanding from the MS inlet must be contained. Hence the Dehmelt potential in existing ion funnels counteracts not only the ion diffusion and Coulomb repulsion, but also the interfering gas drag. A funnel at ambient pressure would experience no such turbulent flow of incoming gas, but only a laminar flow (accelerating toward the exit) due to suction

from the following low-pressure region that actually assists ion transmission. Hence atmospheric-pressure ion focusing may be enabled at lower and  $A$  values than those derived from scaling the parameters of known devices.

Solvated ions such as those generated by ESI require desolvation prior to or at the entrance into a funnel at any pressure. That can be achieved using radiated ion heating or a heated gas bath as employed, e.g., prior to introduction of ESI-generated ions into an ambient-pressure IMS or FAIMS devices.

Microelectrode arrays of desired patterns may be effectively stamped as a single piece on a silicon template and metalized on the surface, e.g., by chemical vapor deposition (CVD). The capacitors and resistors required to form and deploy the necessary RF/DC combinations can be microfabricated on the opposite surface and connected to the metalized strips using masks. Whereas prior ion funnels had curved (conical) internal surfaces, planar ion repelling surfaces are preferred herein given the ease and costs of microfabrication using standard semiconductor processes. Thus, in another key aspect of the invention, ions are confined or focused in one dimension at a time using V-shaped or "wedge" funnels described below. However, the invention is not limited thereto and no limitations are intended by the configurations exemplified herein.

FIGS. 4a-4c show various wedge ion funnel configurations, according to different embodiments of the invention. FIG. 4a shows a longitudinal section and front view of a "wedge" ion funnel 100 comprising two planar sheets 10 disposed at a preselected wedge angle ( $\theta$ ), each configured with electrodes 2 and insulating gaps 4 between them. The value of  $\theta$  can vary, preferably from  $25^\circ$  to  $50^\circ$ . A slit opening 12 is located at the tip of funnel 100. FIG. 4b shows a wedge funnel 100 of the invention followed by a conventional conical funnel that re-focuses ions into a circular beam. Slit 12 can be sufficiently narrow for a pressure of less than  $\sim 30$  Torr in the following differentially pumped chamber, which is low enough for known conventional funnel(s). For example, a wedge funnel 100 with  $g=35$   $\mu$ m and standard 1:1 ratio of electrode 2 and insulating gap 4 widths has  $s=70$   $\mu$ m that allows an exit slit 12 of  $\sim 120$ -140  $\mu$ m width (or 15 times smaller than the exit aperture diameter of funnels known in the art) without undue axial ion trapping. With a practical lateral span of 15 mm, the area of slit 12 would be 1.8-2.1 mm<sup>2</sup>. This essentially equals the 1.7-2.6 mm<sup>2</sup> cross section of multi-inlet capillaries (with up to 19 bores) leading from ambient pressure into ion funnels known in the art. The pressure in those funnels is  $\sim 10$ -30 Torr (depending on the pumping arrangement), and the pressure behind a "wedge" funnel will be similar.

According to another embodiment of the invention, two wedge funnels 100 are placed consecutively as shown in FIG. 4c. Second funnel 100 is rotated  $90^\circ$  around the beam 14 axis relative to first funnel 100. The belt-shaped ion beam 14 leaving the first funnel 100 is refocused into a beam of square or near-circular cross section (cs) after passing the second funnel 100. The implementation of ion funnels, particularly those with microelectrodes, as planar-surface wedge devices, which can be manufactured using existing semiconductor technology and have a sufficiently narrow exit to maintain the pressure in following chamber(s) low enough for conventional funnel operation, is a second key aspect of the invention.

As stated above, the  $w$  and  $A$  values achievable in current funnels are limited by the power constraints of realistic RF waveform sources. To verify that a useful "wedge" funnel is operable using practical power supplies, one can compare its